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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/807,980	07/02/2001	Hiroshi Susaki	P20953	1881

7055 7590 10/31/2003

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EXAMINER	
RUSSEL, JEFFREY E	

ART UNIT	PAPER NUMBER
1654	22

DATE MAILED: 10/31/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/807,980	Applicant(s) SUSAKI ET AL.	
	Examiner Jeffrey E. Russel	Art Unit 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,14-20,22,23 and 26-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *34,35,37 and 38* is/are allowed.

6)☒ Claim(s) *1-11,14-20,22,23,26,28,32 and 33* is/are rejected.

7)☒ Claim(s) *27,29-31 and 36* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 July 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☒ Interview Summary (PTO-413) Paper No(s). *21* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

1. As indicated in the Interview Summary dated October 17, 2003, the finality of the Office action mailed April 17, 2003 has been withdrawn. The restriction requirement between SEQ ID NOS:1 and 8 is withdrawn, and the search has been extended to include both sequences. As a result of the new search, new art is applied against claims 26, 28, 32, and 33. The shortened statutory time period for response is re-started to begin with the mailing of this Office action.

2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

It does not identify the city and either state or foreign country of residence of each inventor. The residence information may be provided on either on an application data sheet or supplemental oath or declaration.

A formal Application Data Sheet will be necessary to correct this defect in the oath. See 37 CFR 1.63(c).

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claims 1-11, 14-20, 22, and 23 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 97/46260 in view of the Japanese Patent Application 6-87746 and Theodore et al (U.S. Patent No. 5,886,143), the Gonsho et al article, the Hashida et al article, the Kichler et al article, or the Nishikawa et al article. (The examiner relies upon the European Patent Application 0 916 348 as a translation of the WO Patent Application '260. All citations in the rejection will use the page, line, and claim numbers of the European Patent Application '348.) The WO Patent Application '260 does not teach a saccharide compound different from the

drug compound bound to the carboxy(C_{1-4})alkyldextran polyalcohol carrier. In particular, the WO Patent Application '260 teaches drug complexes comprising the drug of Applicants' claim 19 (see, e.g., page 5, lines 21-24; page 14, line 36; and claims 7, 14, and 19), which the Japanese Patent Application '746 describes as being useful for treating cancer of the liver (see, e.g., the Abstract), but does not teach incorporating a galactose, galactosamine, or N-acetylgalactosamine residue or cluster thereof into the drug complexes. Theodore et al teach binding hexose clusters and active agents onto polymeric carriers so that the active agents can be targeted for the treatment of liver conditions (see, e.g., column 1, lines 46-64; column 2, lines 27-41; and column 5, lines 13-27). Preferred hexoses include galactose, N-galactosamine, and N-acetylgalactosamine (see, e.g., column 19, lines 44-61 and claim 2). The Gonsho et al article teaches attaching galactose- terminated saccharides such as galactose and N-acetylgalactosamine to a poly(amino acid) in order to form a drug delivery system which targets the liver (see, e.g., the Abstract and page 281, column 2, last paragraph). The Hashida et al article teaches the targeted delivery of drugs and proteins to the liver by attaching galactose moieties to drug carriers (see, e.g., the Abstract; page 129, first paragraph; and page 135, paragraph bridging columns 1 and 2). The Kichler et al article teaches galactose clusters for conjugation to bioactive (macro) molecule carrier systems for targeting the carriers to hepatocytes (see, e.g., the Abstract). The Nishikawa et al article teaches attaching galactose and mannose residues to a carboxymethyl-dextran drug carrier so that a drug conjugated to the carrier can be targeted to liver cells without affinity to other tissues (see, e.g., the Abstract). It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to attach galactose or mannose residues to the drug complexes of the WO Patent Application '260 comprising the drug

of Applicants' claim 19 because the Japanese Patent Application '746 discloses that the drug is useful in treating cancer of the liver and because Theodore et al, the Gonsho et al article, the Hashida et al article, the Kichler et al article, and the Nishikawa et al article teach that attachment of various galactose or mannose residues to polymeric drug carriers is a known and conventional method for targeting drugs to the organ to be treated. It would further have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal galactose or mannose residue:carrier ratios for the above-outlined drug complexes because Theodore et al (see, e.g., column 6, line 15 - column 7, line 16; column 28, lines 18-19), the Hashida et al article (see, e.g., page 133, column 2, second paragraph), and the Gonsho et al article (see, e.g., page 280, Figure 7 and column 2) disclose this ratio to be an art-recognized result-effective variable.

5. Claims 26, 28, 32, and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by the Li et al article (Bioconjugate Chemistry, Vol. 4, pages 275-283). The Li et al article teaches a conjugate which comprises ^{114m}In linked through a chelating agent DOTA and a tetrapeptide linker Gly-Gly-Gly-Phe to an antibody Lym-1. The conjugate is contacted with Cathepsin B, which is a peptidase, and the resulting hydrolysate is measured with a UV detector and a flow-through radioisotope detector. The cathepsin B cleaves the tetrapeptide linker of the conjugate before the phenylalanine residue so that ^{114m}In-DOTA-Gly-Gly-Gly is released. See, e.g., the Abstract; page 278, column 2, first and second full paragraphs; page 279, column 1, fourth full paragraph; and page 281, paragraph bridging columns 1 and 2. The ^{114m}In corresponds to Applicants' drug and antineoplastic agent. The antibody Lym-1 corresponds to Applicants' polymer.

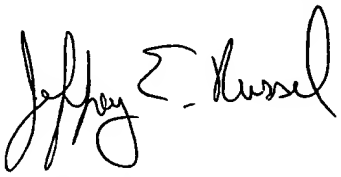
6. Claims 26, 28, 32, and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by the Li et al article (Bioconjugate Chemistry, Vol. 4, pages 275-283) as applied against claims 26, 28, 32, and 33 above, and further in view of Kallman et al (U.S. Patent No. 5,846,974), Saavedra et al (U.S. Patent No. 5,814,656), Terman (U.S. Patent No. 6,340,461), and the Sharma et al article (Anticancer Research, Vol. 17, pages 1815-1822). Kallman et al (see column 13, lines 9-11) and Saavedra et al (see column 11, lines 10-18) are cited to show that antibodies are types of polymers. Terman (see column 80, lines 41-48) is cited to show that ^{114m}In is a radiotherapeutic agent, i.e. a drug. The Sharma et al article (see, e.g., the Abstract) is cited to show that ^{114m}In is useful in the treatment of refractory chronic lymphocytic leukaemia, i.e. is an antineoplastic agent.

7. With respect to the obviousness rejection of claims 1-11, 14-20, 22, and 23 over the WO Patent Application 97/46260 in view of the Japanese Patent Application 6-87746 and Theodore et al (U.S. Patent No. 5,886,143), the Gonsho et al article, the Hashida et al article, the Kichler et al article, or the Nishikawa et al article, the examiner maintains his position for the reasons set forth at page 5, first paragraph, of the Office action mailed April 17, 2003.

8. Claims 34, 35, 37, and 38 are allowed. Claims 27, 29-31, and 36 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (703) 308-3975. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Brenda Brumback can be reached at (703) 306-3220. The fax number for Art Unit 1654 for formal communications is (703) 305-3014; for informal communications such as proposed amendments, the fax number (703) 746-5175 can be used. The telephone number for the Technology Center 1 receptionist is (703) 308-0196.



Jeffrey E. Russel

Primary Patent Examiner

Art Unit 1654

JRussel

October 23, 2003